Association between leptin, body composition, sex and knee cartilage morphology in older adults: the Tasmanian older adult cohort (TASOAC) study

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ABSTRACT

Objective: To describe the associations between leptin, body composition, sex and knee cartilage volume/defects in older adults.

Methods: A cross-sectional sample of 190 randomly selected subjects (mean 63 years, range 52–78, 48% female) were studied. Knee cartilage volume and defects were determined using T1-weighted fat saturation MRI. Serum leptin levels were measured by radioimmunoassay. Fat and lean mass were measured by dual energy *x* ray absorptiometry (DXA). Body mass index (BMI) was calculated.

Results: In multivariable analysis, serum levels of leptin were negatively associated with total cartilage volume (β: −541 mm^3/log transformed unit, 95% CI −861 to −221) but not with prevalent knee cartilage defects. BMI was negatively associated with cartilage volume after adjustment for total lean mass and positively with prevalent knee cartilage defects. However, the association between BMI and cartilage volume disappeared after adjustment for leptin while the association between BMI and cartilage defects remained unchanged. Lastly, sex differences in total cartilage volume decreased substantially after adjustment for leptin (R^2 from 51% to 30%).

Conclusions: This cross-sectional study suggests cartilage volume loss with obesity and female sex is related to leptin and, thus, is hormonally mediated in older adults. By contrast, obesity related knee focal cartilage defects may be more related to non-hormonal factors.

Osteoarthritis (OA) is a slowly progressive disease characterised by gradual loss of articular cartilage with a multifactorial cause. It is well established that obesity and female sex are risk factors for knee OA;[1–3] however, the underlying mechanism remains obscure but may involve biomechanical processes[4] or variations in sex hormones.[2] Although there has been little evidence to show a metabolic link between obesity and knee OA,[3 5] recent hypothetical arguments propose that leptin may represent a systemic factor linking obesity, sex and knee OA.[6 7] Leptin, a 16 kDa non-glycosylated protein encoded by the gene obese (ob), is a hormone secreted mainly by adipocytes[8] as well as osteoblasts and chondrocytes.[7 9] Leptin has been found in the synovial fluid of patients with OA [9 10] and its concentration or mRNA expression in cartilage has been correlated with body mass index (BMI)[9 10] and female sex.[7] However, it is still not clear whether increased production of leptin is good or bad for cartilage health[9 11] with recent evidence suggesting that leptin may act in a biphasic manner,[12] ie, leptin physiologically may have a beneficial effect on cartilage synthesis, but an excess of leptin may lead to detrimental effects on cartilage.[10 12] There are no in vivo data to support this hypothesis to date.

Using MRI, we have demonstrated that BMI is positively associated with knee cartilage defects,[1 13] and fat mass is negatively associated with knee cartilage volume.[14] There are also large sex differences in knee cartilage volume in children[15] and adults[2 16 17] (males have 30–40% higher cartilage volume than females). No studies have reported on whether leptin contributes to the BMI and sex related differences in cartilage morphology. The aim of this cross-sectional study, therefore, was to determine the associations between leptin and knee cartilage volume/defects in older adults, and explore the possible mediating roles of leptin in links between body mass, sex and cartilage volume/defects.

MATERIALS AND METHODS

Subjects

The study was carried out in southern Tasmania, Australia, from March until August 2002. Subjects aged between 50 and 79 years were selected randomly using computer generated random numbers from the electoral roll in southern Tasmania (population 229 000), a comprehensive population listing, with an equal number of men and women. Institutionalised persons were excluded. This study was conducted as part of the Tasmanian Older Adult Cohort (TASOAC) study, an ongoing, prospective, population-based study in 1100 subjects aimed at identifying the environmental, genetic and biochemical factors associated with the development and progression of osteoarthritis and osteoporosis (the overall response rate was 57%). We selected the first 190 subjects to perform serum leptin measurement. The study was approved by the Southern Tasmanian Health and Medical Human Research Ethics Committee, and written informed consent was obtained from all participants. Self-report of smoking status and disease status such as rheumatoid arthritis (RA), asthma, cardiovascular disease and diabetes were recorded by questionnaire.

Anthropometrics

Height was measured to the nearest 0.1 cm (with shoes, socks and headgear removed) using a stadiometer. Weight was measured to the nearest 0.1 kg (with shoes, socks and bulky clothing removed) using a single pair of electronic scales (Seca Delta Model 707, Bradford, Massachusetts,

Table 1 Characteristics of participants

	Leptin < median (n = 96)	Leptin ⩾ median (n = 94)	p Values
Age, years	62.7 (7.2)	62.6 (6.9)	0.916
Female sex, %	17	79	<0.001
Body mass index, kg/m^2	26.0 (3.4)	29.1 (4.7)	<0.001
Total lean mass, kg	57.5 (9.4)	47.8 (10.0)	<0.001
Total fat mass, %	28.2 (4.7)	39.2 (5.9)	<0.001
Trunk fat mass, %	27.8 (5.3)	38.3 (5.7)	<0.001
Current smokers, %	17	15	0.889
Rheumatoid arthritis, %	8	14	0.227
Asthma, %	6	24	0.001
Cardiovascular diseases, %	5	3	0.489
Diabetes, %	3	8	0.182
Knee pain, %	40	53	0.071
Medial joint space narrowing, %	48	56	0.266
Lateral joint space narrowing, %	16	15	0.923
Medial tibiofemoral osteophytes, %	7	7	0.952
Lateral tibiofemoral osteophytes, %	3	3	0.967
Prevalent medial cartilage defects, %	25	22	0.543
Prevalent lateral cartilage defects, %	19	17	0.622
Prevalent patellar cartilage defects, %	34	44	0.194
Prevalent total cartilage defects, %	46	54	0.246
Total cartilage defects, 0–20	5.7 (2.4)	6.0 (1.9)	0.506
Medial tibial cartilage volume, ml	3.0 (0.3)	2.4 (0.5)	<0.001
Lateral tibial cartilage volume, ml	3.4 (0.7)	2.6 (0.5)	<0.001
Patellar cartilage volume, ml	3.9 (0.9)	3.1 (0.8)	<0.001
Total cartilage volume, ml	10.2 (1.6)	8.0 (1.5)	<0.001

Data shown are mean (SD) or median (interquartile range), except for percentages. Median value of leptin: 8.7 μg/litre.

USA) that were calibrated using a known weight at the beginning of each clinic. The body mass index (BMI; weight (kg)/height (m^2)) was calculated. Fat mass and lean mass (kg) were measured by a Hologic dual energy *x* ray absorptiometry (DXA) scanner (Hologic Corp., Waltham, Massachusetts, USA). Percentage total body or trunk fat mass is the ratio of total body or trunk fat mass divided by total body or trunk mass (ie, the sum of fat mass, lean mass and bone mass).

x Ray and knee pain assessment

A standing anteroposterior semiflexed view of the right knee with 15° of fixed knee flexion was performed in all subjects at baseline and scored individually for osteophytes and joint space narrowing on a scale of 0–3 (0 = normal and 3 = severe) according to the Osteoarthritis Research Society International (OARSI) atlas as previously described.[18] The presence of radiographic OA (ROA) was defined as any score of ⩾1.

Knee pain (on flat surface, going up/down stairs, at night, sitting/lying and standing upright) was assessed by self-administered questionnaire using the Western Ontario McMaster Osteoarthritis Index (WOMAC) with a 10-point scale from 0 (no pain, stiffness or no function problems) to 9 (most severe pain, stiffness or severe function problems).[19] Each score of knee pain was summed to create a total pain (0–45) score. Prevalent knee pain was defined as a total score of ⩾1.

Knee cartilage volume measurement

Knee cartilage volume was determined by means of image processing on an independent workstation as previously described.[15 20] The volumes of individual cartilage plates (medial tibial, lateral tibial and patella) were isolated from the total volume by manually drawing disarticulation contours around the cartilage boundaries on a section by section basis. These data were then resampled by means of bilinear and cubic interpolation (area of 312 and 312 μm and 1.5 mm thickness, continuous sections) for the final 3D rendering. The coefficients of variation (CVs) for cartilage volume measures were 2.1–2.6%. The sum of medial tibial, lateral tibial and patellar cartilage volume was regarded as "total" cartilage volume.

Cartilage defects (0–4 scale) were graded at medial tibial, medial femoral, lateral tibial, lateral femoral and patellar sites as follows:[13 21] grade 0, normal cartilage; grade 1, focal blistering and intracartilaginous low-signal intensity area with an intact surface and bottom; grade 2, irregularities on the surface or bottom and loss of thickness of less than 50%; grade 3, deep ulceration with loss of thickness of more than 50%; grade 4, full-thickness chondral wear with exposure of subchondral bone. A cartilage defect also had to be present in at least two consecutive slices. A prevalent cartilage defect was defined as

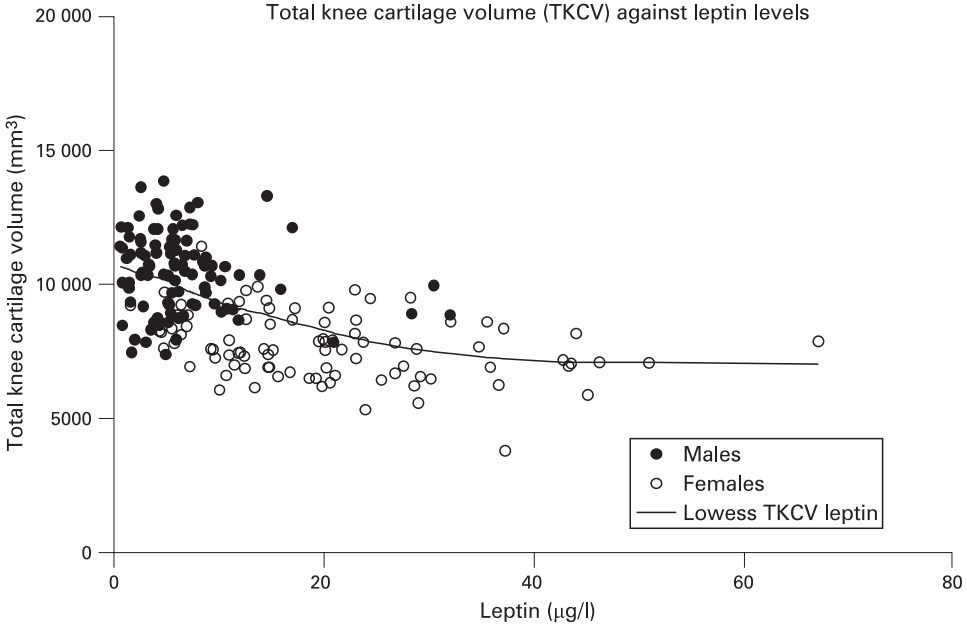

Figure 1 Scatter-plot for the association between serum levels of leptin and total knee cartilage volume. Log transformed leptin was significantly associated with knee cartilage volume ($r = -0.52$, $p<0.001$) in unadjusted analysis.

Table 2 Associations between leptin, knee cartilage volume and cartilage defects

	Univariable	Multivariable*
Cartilage volume, β (95% CI):		
Total	**–1028 (–1270 to –787)**	**–541 (–861 to –221)**
Medial tibial	**–298 (–375 to –221)**	**–183 (–300 to –66)**
Lateral tibial	**–350 (–441 to –259)**	**–161 (–294 to –28)**
Patellar	**–380 (–501 to –260)**	**–183 (–340 to –26)**
Cartilage defects, odds ratio (95% CI):		
Total	1.13 (0.84 to 1.51)	0.89 (0.52 to 1.52)
Medial tibiofemoral	0.91 (0.65 to 1.28)	0.60 (0.32 to 1.13)
Lateral tibiofemoral	1.01 (0.69 to 1.16)	1.09 (0.54 to 2.23)
Patellar	1.15 (0.85 to 1.55)	0.73 (0.43 to 1.23)

Dependent variable: cartilage volume, mm^3 or prevalent castilage defects. Independent variable: leptin, per unit. Data in bold denotes a statistically significant result.
*Adjusted for sex, age, body mass index (BMI), smoking, knee joint space narrowing, osteophytes, rheumatoid arthritis (RA), asthma, cardiovascular diseases and cartilage defects if cartilage volume or cartilage volume if cartilage defects.

a cartilage defect score of ⩾2 at any site within that compartment. Intraobserver reliability (expressed as intraclass correlation coefficient (ICC)) was 0.89–0.94 and interobserver reliability was 0.85–0.93.[21]

Tibial bone area at the medial and lateral compartments was determined as previously described.[18]

Serum leptin measurement

Serum was separated and aliquotted into plastic storage tubes. Aliquots were stored at –80°C till analysis. The levels of leptin were measured by radioimmunoassay (LINCO Research; now part of Millipore, Missouri, USA). Samples with undetectable leptin concentration were assigned a value corresponding to the lower limit of detection of the assay (0.5 μg/litre). The intra and inter assay CVs were 4.6% and 5% respectively in our hands

Data analysis

Student t or χ^2 tests (where appropriate) were used to compare means. A scatter plot and locally weighted scatterplot smoothing (lowess) plot were used to depict the association between unadjusted leptin levels and total knee cartilage volume. The lowess command models the data locally using a cubic weighted least squares regression, with weights that give more importance to local data points. Leptin was not normally distributed, hence was log transformed for analyses. Univariable and multivariable linear regression analyses were used to examine the associations between knee cartilage volume and log transformed leptin before and after adjustment age, sex, BMI, smoking status, ROA, bone size, other disease status (RA, cardiovascular disease, asthma and diabetes). The associations between knee cartilage volume and BMI (or body fat mass) were also investigated by linear regression after adjustment for leptin. Similarly, univariable and multivariable logistic regression analyses were used to examine the associations between prevalent knee cartilage defects and log transformed leptin/BMI/body fat mass. Standard diagnostic checks of model fit and residuals were routinely made, and data points with large residuals and/or high influence were investigated for data errors. A p value <0.05 (two-tailed) or a 95% confidence interval not including the null point were regarded as statistically significant. All statistical analyses were performed on SPSS V.12.0 for Windows (SPSS, Chicago, Illinois, USA) or Stata statistical software, V.9.2 (Stata Corp., College Station, Texas, USA).

RESULTS

A total of 190 subjects (48% female) aged between 52 and 78 (mean 63 years) participated in the present study. There were no significant differences in demographic factors and knee cartilage volume between the current cohort and the subjects who did not have serum markers measured (mean (SD) age: 62.6 (7.1) vs 62.3 (7.5) years, $p = 0.57$; female sex: 48% vs 50%, $p = 0.62$; BMI: 27.5 (4.4) vs 27.7 (4.5) kg/m^2, $p = 0.68$; and total cartilage volume: 9.1 (1.9) vs 9.2 (1.8) ml, $p = 0.42$). This is a mixed population with 58% subjects having radiographic changes (joint space narrowing or osteophytes score of ⩾1) in the right knee and 46% having knee pain. Characteristics of the subjects are presented in table 1. Subjects with higher and lower levels of leptin (split at the median of 8.7 μg/litre) were similar in terms of age, smoking status, knee pain, radiographic joint space narrowing, osteophytes, prevalent cartilage defects and

Table 3 Associations between BMI, knee cartilage volume and cartilage defects: mediating roles of leptin

	Univariable	Multivariable*	Multivariable†	Multivariable‡
Cartilage volume, β (95% CI):				
Total cartilage	–48 (–112 to 16)	**–99 (–144 to –53)**	**–51 (–98 to –4)**	–2 (–61 to 56)
Medial tibial cartilage	–14 (–34 to 6)	**–27 (–43 to –11)**	–14 (–32 to 3)	+3 (–19 to 24)
Lateral tibial cartilage	**–24 (–47 to –0.4)**	**–40 (–58 to –21)**	**–26 (–45 to –6)**	–9 (–34 to 15)
Patellar cartilage	–10 (–40 to 20)	**–31 (–55 to –8)**	–21 (–47 to 4)	–10 (–42 to 23)
Cartilage defects, odds ratio (95% CI):				
Total cartilage	1.06 (0.99 to 1.13)	–	**1.10 (1.01 to 1.19)**	**1.12 (1.01 to 1.24)**
Medial tibiofemoral cartilage	1.04 (0.96 to 1.12)	–	1.04 (0.94 to 1.14)	1.10 (0.98 to 1.25)
Lateral tibiofemoral cartilage	1.01 (0.93 to 1.10)	–	1.01 (0.91 to 1.11)	1.00 (0.87 to 1.15)
Patellar cartilage	**1.08 (1.01 to 1.16)**	–	**1.14 (1.06 to 1.24)**	**1.19 (1.07 to 1.32)**

Dependent variable: cartilage volume, mm^3 or prevalent cartilage defects. Independent variable: body mass index (BMI), kg/m^2. Data in bold denotes a statistically significant result.
*Adjusted for total lean mass; †further adjusted for sex, age, smoking, knee joint space narrowing, osteophytes, rheumatoid arthritis (RA), asthma, diabetes and cardiovascular diseases; ‡further adjusted for leptin.

Table 4 Associations between body composition and knee cartilage volume: mediating roles of leptin

	Univariable	Multivariable*	Multivariable†
Total cartilage, β (95% CI):			
Trunk fat, %	**–147 (–177 to –116)**	**–98 (–154 to –42)**	**–75 (–134 to –16)**
Total fat, %	**–173 (–199 to –146)**	**–111 (–185 to –38)**	**–80 (–156 to –5)**
Medial tibial cartilage, β (95% CI):			
Trunk fat, %	**–41 (–51 to –31)**	**–31 (–50 to –11)**	**–22 (–43 to –2)**
Total fat, %	**–47 (–56 to –38)**	**–31 (–57 to –5)**	–20 (–47 to 7)
Lateral tibial cartilage, β (95% CI)			
Trunk fat, %	**–51 (–63 to –40)**	**–32 (–54 to –10)**	**–27 (–51 to –3)**
Total fat, %	**–59 (–69 to –49)**	**–42 (–72 to –13)**	**–35 (–66 to –5)**
Patellar cartilage, β (95% CI):			
Trunk fat, %	**–54 (–70 to –39)**	**–37 (–63 to –11)**	**–30 (–58 to –2)**
Total fat, %	**–66(–80 to –52)**	**–46 (–81 to –10)**	–35 (–72 to 2)

Dependent variable: cartilage volume, mm^3. Independent variable: trunk fat, or total fat mass. Data in bold denotes a statistically significant result.
*Adjusted for sex, age, body mass index (BMI), smoking, knee joint space narrowing, osteophytes, rheumatoid arthritis (RA), asthma and cardiovascular diseases; †further adjusted for leptin.

total cartilage defect scores. However, subjects with higher levels of leptin had a higher proportion of female sex, greater BMI, less lean mass and greater % fat mass, higher prevalence of asthma and lower cartilage volume.

Leptin levels were significantly associated with knee cartilage volume before (fig 1, table 2) and after adjustment for sex, age, BMI, smoking, ROA, cartilage defects and other disease status. The associations remained largely unchanged after further adjustment for tibial bone size. By contrast, no significant associations were determined between prevalent cartilage defects and leptin in univariable and multivariable analyses (table 2).

BMI was significantly associated with leptin before and after adjustment for covariates (partial $r = 0.62$, $p<0.001$) in this sample. In table 3, although most associations between BMI and knee cartilage volume in the univariable analyses were not significant, BMI was significantly negatively associated with knee cartilage volume after adjustment for lean mass (as total lean mass was positively associated with total cartilage volume ($p<0.001$)). The associations between BMI, and total and lateral tibial cartilage volume remained significant after further adjustment for other covariates; however, these associations became non-significant after further adjustment for leptin (table 3). In addition, BMI was significantly positively associated with prevalent total and patellar cartilage defects but, in contrast, these associations did not change after further adjustment for leptin (table 3).

Percentage total fat and trunk fat mass was also positively associated with leptin in multivariable analyses (partial $r = 0.31$ and $r = 0.36$, respectively, both $p<0.001$). In table 4, percentage total fat mass and trunk fat mass were negatively associated with knee cartilage volume. These associations decreased by 25–30% after adjustment for leptin (table 4). By contrast, there were no significant association between fat mass and knee cartilage defects, and these associations were not altered by further adjustment for leptin (data not shown).

There were large sex differences in leptin levels (women vs men: +12 μg/litre, $R^2 = 43\%$, $p<0.001$) and total knee cartilage volume ($R^2 = 51\%$, table 5). The sex difference in total knee cartilage volume decreased substantially in magnitude but remained significant after adjustment for leptin ($R^2 = 30\%$) (table 5). The association between sex and prevalent total cartilage defects was not significant in this sample (OR = 1.20, $p = 0.60$), and was not influenced by adjustment for leptin.

No significant association was present between leptin and ROA in adjusted analysis (data not shown). Subjects with higher leptin levels had a trend to higher prevalence of knee pain and medial joint space narrowing (JSN) but these were not significant (table 1). The association between leptin and medial JSN (OR = 1.10, $p = 0.65$) remained unchanged after adjustment for knee pain (OR = 1.07, $p = 0.76$). The strength of the associations and the evidence of mediation by leptin did not differ when the analysis were performed separately in men and women (data not shown). No significant interaction was present between sex and leptin ($p = 0.92$) or radiographic OA and leptin ($p = 0.64$) for total cartilage volume, so all data were combined for analyses. Results remained largely unchanged when subjects with RA, cardiovascular diseases, diabetes, or asthma were excluded for analyses (data not shown).

Table 5 Associations between sex and knee cartilage volume: mediating roles of leptin

	Univariable	Multivariable*	Multivariable†
	β (95% CI)/R^2	**β (95% CI)/partial R^2**	**β (95% CI)/partial R^2**
Total cartilage	−2764 (−3154 to −2374)/R^2: 51%	−2669 (−3076 to −2261)/R^2: 51%	−2174 (−2694 to −1654)/R^2: 30%
Medial tibial cartilage	−763 (−896 to −629)/R^2: 40%	−704 (−847 to −560)/R^2: 37%	−531 (−715 to −348)/R^2: 17%
Lateral tibial cartilage	−909 (−1066 to −752)/R^2: 41%	−861 (−1025 to −697)/R^2: 40%	−699 (−910 to −489)/R^2: 21%
Patellar cartilage	−1092 (−1300 to −885)/R^2: 36%	−1046 (−1265 to −828)/R^2: 34%	−909 (−1196 to −621)/R^2: 18%

Dependent variable: cartilage volume, mm^3. Independent variable: sex (men = 0, women = 1). All results were statistically significant.
*Adjusted for age, body mss index (BMI), smoking, knee joint space narrowing, osteophytes, rheumatoid arthritis (RA), asthma, diabetes and cardiovascular diseases; †further adjusted for leptin.

DISCUSSION

This study reports a consistent negative association between serum leptin levels and knee cartilage volume (both total and in all compartments) in older adults with or without radiographic OA. This was independent of BMI and sex. Conversely, the associations between BMI, body fat mass, sex and knee cartilage volume were not independent of serum leptin levels. Lastly, the association between BMI and prevalent knee cartilage defects was not related to leptin.

Assessment of cartilage volume and cartilage defects by MRI, with fat-suppressed gradient echo sequences, and appropriate image analysis techniques, has high accuracy and adequate precision for cross-sectional and longitudinal studies in healthy subjects and patients with OA.[22 23] Cartilage defects and volume are both important in OA. Cartilage defects seem to represent an early stage of cartilage damage and predict cartilage volume loss in a number of studies.[23] Independent to the association with cartilage defects, cartilage volume is also impacted on by other structural and, based on this study, hormonal factors. We found that higher serum leptin levels were significantly associated with lower knee cartilage volume at all three sites. This is in line with a recent in vitro study that suggested that leptin and its receptor (ob-Rb) mRNA was expressed at significantly higher levels in osteoarthritic compared to normal cartilage, and leptin had a detrimental effect on chondrocyte proliferation and induced matrix metalloproteinase (MMP) 9 and 13 protein expression.[10] Although studies suggest that leptin levels are higher in synovial fluid than in serum,[10 24] our data clearly demonstrates that serum leptin levels are associated with reduced knee cartilage volume in one knee, suggesting a systemic hormonal influence on cartilage volume. Whether this reflects a systemic effect on other joints with hyaline cartilage is unknown, but is deserving of further study. The associations between leptin and knee cartilage volume remained significant after adjustment for BMI, suggesting its effects on knee cartilage are independent of BMI. Of note, we found that medial joint space narrowing scores were worse in subjects with high leptin levels (>median value) but this was not significant, most likely indicating lower sensitivity for radiographs compared with MRI. A more sensitive protocol for the radiography, eg, the Lyon schuss view, may show such a difference or it may be that all radiographs lack sensitivity.

Consistent with our previous report,[1] BMI was not significantly associated with knee cartilage volume in unadjusted analysis. However, BMI was significantly negatively associated with knee cartilage volume when the protective effect of lean mass was taken into account (by adjustment for lean mass). Similarly, fat mass was negatively associated with knee cartilage volume, which is also consistent with a recent report.[14] The associations of BMI and fat mass with cartilage volume were dependent on leptin, suggesting that at least some of the association between obesity and cartilage volume is hormonally linked rather than purely mechanical. By contrast, we did not find significant associations between serum leptin and knee focal cartilage defects even though cartilage defects were significantly associated with loss of cartilage volume.[23] Although obesity was associated with cartilage defects as we have previously reported,[1] adjustment for leptin did little to this suggesting cartilage splitting or focal defects are more susceptible to mechanical loading[25] than hormonal effects.

Males have consistently higher knee cartilage volumes than females,[15–17 26] as seen in the findings from this study. This is predominantly due to greater body size. Other factors may include sex hormones and growth factors.[16] Variation in leptin may be another contributor. Indeed, we found that older females had significantly greater serum leptin levels than older males, and sex differences in knee cartilage volume decreased substantially in magnitude after adjustment for leptin providing support for this hypothesis.

Our study has several potential limitations. First, the sample size was relatively small, which may miss moderate associations; however, significant associations between leptin and knee cartilage volume were detected using this sample size. Second, the response rate at baseline was 57%, which may leave the possibility open for selection bias although there were no differences between those reported in this study and the rest of the cohort. Third, this randomly selected sample contained subjects with other diseases. However, the results were largely unchanged when the analyses were adjusted for disease status or these subjects were excluded. Fourth, we used tibial cartilage as the measure of joint cartilage at the tibiofemoral joint rather that femoral cartilage, and it is possible that associations with femoral cartilage are different to those with tibial cartilage.[27] However, we have previously shown a strong correlation between the tibial and femoral cartilage in the medial and lateral tibiofemoral compartments.[28] It would be worthwhile to examine associations at other sites, eg, hip and spinal discs. Fifth, measurement error may influence results. However, all measures were highly reproducible suggesting this is unlikely. Lastly, due to cross-sectional nature, this study cannot exclude the possible confounding effect on cartilage volume measurements of hypertrophic repair or swelling in OA cartilage. The cause effect relationship between obesity, sex, leptin and cartilage needs to be elucidated by longitudinal studies.

In conclusion, this cross-sectional study suggests that cartilage volume loss with obesity and female sex is related to leptin and, thus, is hormonally mediated in older adults. By contrast, obesity related knee focal cartilage defects may be more related to non-hormonal factors.

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Competing interests: None.

Ethics approval: The study was approved by the Southern Tasmanian Health and Medical Human Research Ethics Committee, and written informed consent was obtained from all participants.

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